$$\text{Micrograms of cefotiam per milligram} = \frac{A_u \times P_s \times 100}{A_s \times C_u \times (100 - L - S)}$$

where:

A_u=Area of the cefotiam peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s=Area of the cefotiam peak in the chromatogram of the cefotiam working standard;

P_s=Cefotiam activity in the cefotiam working standard solution in micrograms per milliliter;

C_u=Milligrams of the sample per milliliter of sample solution;

L=Percent loss on drying (determined as directed in paragraph (b)(4) of this section); and

S=Percent sodium carbonate (determined as directed in paragraph (b)(6) of this section).

(B) *Cefotiam content (milligrams of cefotiam per vial).* Calculate the cefotiam content of the vial as follows:

$$\text{Milligrams of cefotiam per vial} = \frac{A_u \times P_s \times d}{A^s \times 1{,}000}$$

where:

A_u=Area of the cefotiam peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s=Area of the cefotiam peak in the chromatogram of the cefotiam working standard;

P_s=Cefotiam activity in the cefotiam working standard solution in micrograms per milliliter; and

d=Dilution factor of the sample.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(g) of this chapter, using a solution containing 40 milligrams of cefotiam per milliliter.

(4) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(6) *Sodium carbonate content.* Proceed as directed in § 436.357 of this chapter.

[54 FR 20786, May 15, 1989]

§ 442.260 Cefpiramide sodium for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefpiramide sodium for injection is a dry mixture of cefpiramide and sodium benzoate. It contains other buffers and preservatives. Its cefpiramide potency is satisfactory if each milligram of cefpiramide sodium for injection contains not less than 754 micrograms and not more than 924 micrograms of cefpiramide on an anhydrous basis. Its cefpiramide content is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams of cefpiramide that it is represented to contain. It is sterile. It is nonpyrogenic. Its moisture content is not more than 3.0 percent. Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 6.0 and not more than 8.0. It passes the identity test. The cefpiramide used conforms to the standards prescribed by § 442.60(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The cefpiramide used in making the batch for potency, moisture, pH, total related substances, specific rotation, identity, and crystallinity.

(B) The batch for cefpiramide potency, cefpiramide content, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples, if required by the Center for Drug Evaluation and Research:

(A) The cefpiramide used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Cefpiramide potency and content.* Determine both micrograms of cefpiramide per milligram of sample and milligrams of cefpiramide per container.

Proceed as directed in § 442.60(b)(1), preparing the sample solutions and calculating the potency and content as follows:

(i) *Preparation of sample solutions.* Use separate containers for preparation of each sample solution as described in paragraphs (b)(1)(i)(A) and (b)(1)(i)(B) of this section.

(A) *Cefpiramide potency (micrograms of cefpiramide per milligram*). Dissolve an accurately weighed sample with sufficient mobile phase to obtain a solution containing approximately 0.25 milligram of cefpiramide per milliliter (estimated).

(B) *Cefpiramide content (milligrams of cefpiramide per vial*). Reconstitute the sample as directed in the labeling. Then, using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute the solution thus obtained with sufficient distilled water to obtain a solution containing 1.0 milligram of cefpiramide activity per milliliter (estimated). Further dilute this solution with mobile phase to obtain a solution containing 0.25 milligram of cefpiramide activity per milliliter (estimated).

(ii) *Calculations*—(A) *Cefpiramide potency (micrograms per milligram*). Calculate the micrograms of cefpiramide per milligram as follows:

$$\text{Micrograms of cefpiramide per milligram} = \frac{A_u \times P_s \times 100}{A_s \times C_u \times (100 - m)}$$

where:

A_u=Area of the cefpiramide peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s=Area of the cefpiramide peak in the chromatogram of the cefpiramide working standard;

P_s=Cefpiramide activity in the cefpiramide working standard solution in micrograms per milliliter;

C_u=Milligrams of the sample per milliliter of sample solution;

m =Percent moisture content of the sample.

(B) *Cefpiramide content (milligrams of cefpiramide per vial).* Calculate the cefpiramide content of the vial as follows:

$$\text{Milligrams of cefpiramide per vial} = \frac{A_u \times P_s \times d}{A_s \times 1{,}000}$$

where:

A_u=Area of the cefpiramide peak in the chromatogram of the sample (a ta retention time equal to that observed for the standards);

A_s=Area of the cefpiramide peak in the chromatogram of the cefpiramide working standard;

P_s=Cefpiramide activity in the cefpiramide working standard solution in micrograms per milliliter; and

d=Dilution factor of the sample.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in § 436.20(e)(1).

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 50 milligrams of cefpiramide per milliliter.

(4) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(6) *Identify.* The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the cefpiramide working standard.

[55 FR 14242, Apr. 17, 1990]

§ 442.270 Cefmetazole injectable dosage forms.

§ 442.270a Sterile cefmetazole sodium.

The requirements for certification and the tests and methods of assay for sterile cefmetazole sodium packaged for dispensing are described in § 442.70a.

[55 FR 6636, Feb. 26, 1990]

§ 442.270b Cefmetazole sodium injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefmetazole sodium injection is a frozen, aqueous, iso-osmotic solution of cefmetazole and sodium citrate. It contains one or more suitable